The 7th International Electronic Conference on Medicinal Chemistry (ECMC 2021)
01–30 NOVEMBER 2021 | ONLINE

# Bioformulations of Sage-Aloe Vera-PVP and "smart" triiodides with antimicrobial properties

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جامعة عجمان
AJMAN UNIVERSITY

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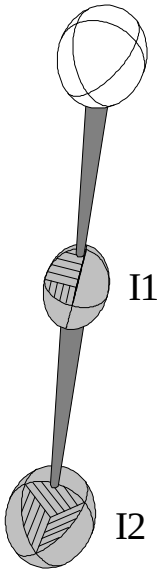
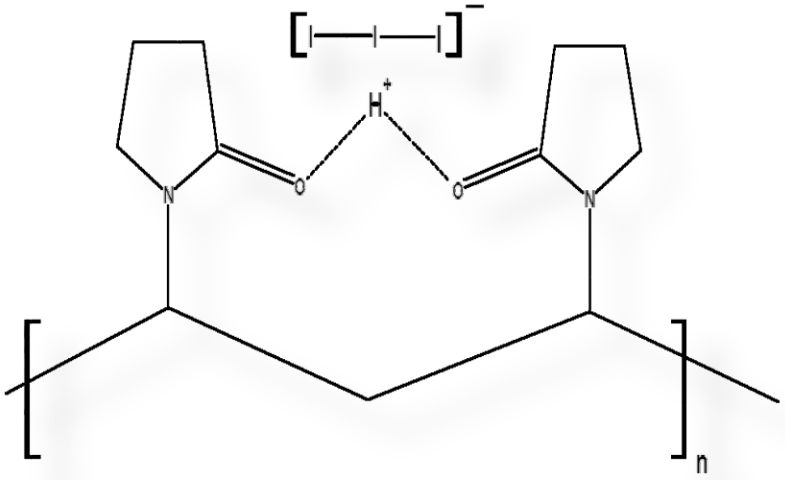
## Graphical Abstract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**Abstract:**
The worldwide Covid-19 pandemic highlighted the importance of developing new generation of sustainable, low-cost and easy accessible bio-antimicrobial agents. The worldwide confusion and pressure on the health care systems, overwhelmed healthcare workers, peaking mortality rates and suffering in emergency rooms traumatized the world population. Enforced isolation, standstill of all normal daily activities, the sudden lack of basic drugs and commodities even in industrial countries left scars in the human mind. There is an urgent need for remedies, known since centuries and available in every household as alternative bioantimicrobials against multidrug resistant ESKAPE pathogens. We prepared formulations of well known microbicides *Aloe Vera Barbadensis Miller* (AV), *Salvia officinalis* (Sage) and iodine ($I_2$) and stabilized them with polyvinylpyrrolidone (PVP). These biohybrids were tested against 10 pathogens on discs and polyglycolic acid (PGA) surgical sutures by disc diffusion methods. Our bioformulations showed excellent to intermediate inhibitory action against our selection of microorganisms on discs and sutures. AV-PVP-Sage-$I_2$ biocompounds can be used as low-cost, non-toxic microbicides, disinfectants and agents to stop surgical site infections.
**Keywords:** Antimicrobial resistance; Aloe Vera; Sage; Iodine; biohybrids

## Introduction

**New classes** of antimicrobial agents based on **natural plant extracts** offer valuable solutions due to their **naturally evolved synergistic mechanisms** **in the fight against microorganisms.**

***Aloe Vera*-biosynthesized composites within smart triiodides** may have potential for developing new generation antibiotics and antimicrobials. These materials may disable microbial defense mechanisms, which usually lead to resistance.

**Our compounds are easily accessible, one-pot, bio-synthesized biopolymers with iodine.**

## Introduction

**Medicinal/herbal plants** are sources of **phenolic acids, polyphenols, flavonoids, terpenoids and further phytochemicals**.

**Phytochemicals** can reduce biofilm formation inhibit quorum sensing, prevent bacterial attachment on mucosal surfaces, cell surface hydrophobicity and glycolytic enzymes.

**Aloe Vera** and **Sage** contain many phytochemicals and therefore are excellent alternatives for drug development.

The antimicrobial activity of plant constituents is ruled by morphology and structure of the target pathogens.

This finding is in agreement with our previous investigations on complexes of **"smart" triiodides, which were produced with the addition of molecular iodine ($I_2$)**.

## Results and discussion

In this work, we encapsulated **freshly extracted AV gel** **with polyvinylpyrrolidone (PVP) and incorporated iodine ($I_2$), as well as *Salvia officinalis* L. *(Sage)* into the polymer matrix.**

- **AV-PVP-Sage-$I_2$ formulations** and their dip-coated PGA sutures were tested against **10 reference strains of microorganisms**
- compared to the **antibiotics gentamycin and nystatin**
- by zone inhibition with disc-diffusion methods.

## Results and discussion

We soaked

2 mL of AV-PVP-Sage-$I_2$ with concentrations of

11 µg/mL,

5.5 µg/mL,

2.75, and

1.38 µg/mL

on sterile filter paper discs for 18 h and dried them for 24 h under ambient conditions.

We impregnated

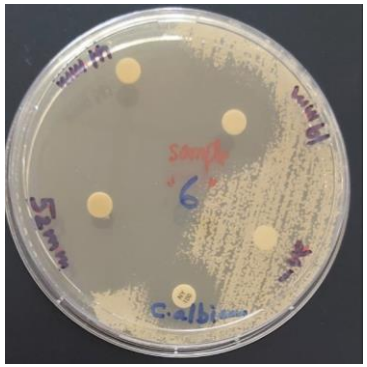
multifilamented, sterile PGA (polyglycolic acid) sutures into 50 mL of AV-PVP-Sage-$I_2$ solution with a concentration of

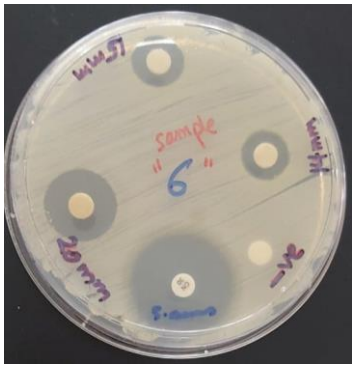
11 µg/mL

at 25 °C and for 18 h

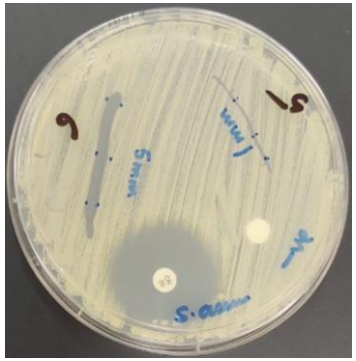
dried them for 24 h under ambient conditions.

# Results and discussion








| Strain | Antibiotic | A | 1 [+] | 2 [+] | 3 [+] | S |
|---|---|---|---|---|---|---|
| S. pneumoniae ATCC 49619 | G | 18 | **14** | **11** | **10** | **3** |
| S. aureus ATCC 25923 | G | 28 | **20** | **15** | **14** | **5** |
| S. pyogenes ATCC 19615 | G | 25 | 14 | 12 | 10 | 2 |
| E. faecalis ATCC 29212 | G | 25 | **15** | **12** | **10** | **2** |
| B. subtilis WDCM 00003 | G | 21 | **13** | **12** | **11** | **3** |
| P. mirabilis ATCC 29906 | G | 30 | 0 | 0 | 0 | 0 |
| P. aeruginosa WDCM 00026 | G | 23 | 0 | 0 | 0 | 0 |
| E. coli WDCM 00013 | G | 23 | 11 | 0 | 0 | 1 |
| K. pneumoniae WDCM 00097 | G | 30 | 13 | 9 | 0 | 2 |
| C. albicans WDCM 00054 | NY | 16 | **52** | **41** | **19 *** | **15** |

[+] Disc diffusion studies (6 mm disc impregnated with 2 mL of 11 μg/mL (1), 2 mL of 5.5 μg/mL (2) and 2 mL of 2.75 μg/mL (3) of AV-PVP-Sage-$I_2$. A = G Gentamicin (30 μg/disc). NY (Nystatin) (100 IU). S suture and M mask tissue dip-coated with 2 mL of 17 μg/mL AV-PVP-Sage-$I_2$. Grey shaded area represents Gram-negative bacteria. 0 = Resistant. * Further dilution to 1.38 μg/mL yielded ZOI = 10 mm. No statistically significant differences ($p > 0.05$) between row-based values through Pearson correlation.

## Results and discussion

- **AV-PVP-Sage-$I_2$ formulations** showed excellent to intermediate antimicrobial activity in discs and sutures.
- The **iodine** within the polymeric biomaterial AV-PVP-Sage-$I_2$ and the **synergistic action** of the **two plant extracts** enhanced the microbial inhibition.

## Conclusions

- **AV-PVP-Sage-$I_2$ formulations** have strong potential for use as an **antifungal agent** **against *C. albicans***
- **disinfectant** **especially against Gram-positive bacteria**
- **coating material on sutures** to prevent surgical site infections.
- **Smart bio-antimicrobials** are interesting alternatives as **sustainable basic disinfectants and coating materials.** Such biomaterials may serve the public during health care system failures.
-

## Conclusions

**Smart materials** based on synergistic antimicrobial action are interesting **alternatives against resistant microorganisms**.

We proved, that our compounds have **strong antifungal** as well as antibacterial activity against **Gram-positive pathogens**.

We confirmed the composition of AV-PVP-Sage-$I_2$ by UV-Vis, FT-IR, Raman, XRD and microstructural analysis by SEM/EDS.

Important factors are stability and long-term effectiveness of the new compounds. The **controlled, slow release of free Iodine**, as well as iodide ions, enhance the antimicrobial activity.

## Conclusions

**Plant Polyphenols incorporated into polymer or complex matrices** have been tested as **antimicrobial agents** in several studies. These hybrids enhance the antimicrobial activity on microorganisms.

**Our compounds are easily accessible, one-pot, bio-synthesized biopolymers with iodine.**

Our hybrids can be used to coat sutures to **prevent** the development of **Surgical Site Infections (SSI)**.

# Acknowledgements


- **Ajman University**
- Center of Medical and Bio-allied Health Sciences Research, Ajman University
- **Deanship of Graduate Studies and Research**, AU, Ajman, United Arab Emirates
- **Artist "@art_by_amie_"** for providing us with digital art images as graphical abstracts for our publications
- All our colleagues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biomimetics

MDPI

*Article*

## Facile Synthesis of Antimicrobial Aloe Vera-"Smart" Triiodide-PVP Biomaterials

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Received: 27 August 2020; Accepted: 11 September 2020; Published: 17 September 2020

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**Abstract:** Antibiotic resistance is an eminent threat for the survival of mankind. Nosocomial infections caused by multidrug resistant microorganisms are a reason for morbidity and mortality worldwide. Plant-based antimicrobial agents are based on synergistic mechanisms which prevent resistance and have been used for centuries against ailments. We suggest the use of cost-effective, eco-friendly *Aloe Vera Barbadensis* Miller (AV)-iodine biomaterials as a new generation of antimicrobial agents. In a facile, one-pot synthesis, we encapsulated fresh AV gel with polyvinylpyrrolidone (PVP) as a stabilizing agent and incorporated iodine moieties in the form of iodine ($I_2$) and sodium iodide (NaI) into the polymer matrix. Ultraviolet-visible spectroscopy (UV-Vis), Fourier transform infrared spectroscopy

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International Journal of
*Environmental Research and Public Health*

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*Article*

## A Look Behind the Scenes at COVID-19: National Strategies of Infection Control and Their Impact on Mortality

**Samir Haj Bloukh [1], Zehra Edis [2,*], Annis A. Shaikh [3] and Habib M. Pathan [3]**

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Received: 9 July 2020; Accepted: 28 July 2020; Published: 4 August 2020

check for updates

**Abstract:** (1) Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began spreading across the globe in December and, as of 9 July 2020, had inflicted more than 550,000 deaths. Public health measures implemented to control the outbreak caused socio-economic havoc in many countries. The pandemic highlighted the quality of health care systems, responses of policymakers in harmony with the population, and socio-economic resilience factors. We suggest that different national strategies had an impact on mortality and case count. (2) Methods: We collected fatality data for 17 countries until 2 June 2020 from public data and associated these with implemented containment measures. (3) Results: The outcomes present the effectiveness of control mechanisms in mitigating the virus for selected countries and the UAE as a special case. Pre-existing conditions defined

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*pharmaceutics*

MDPI

*Article*

## "Smart" Antimicrobial Nanocomplexes with Potential to Decrease Surgical Site Infections (SSI)

**Zehra Edis [1,*], Samir Haj Bloukh [2], May Reda Ibrahim [1] and Hamed Abu Sara [2]**

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Received: 10 March 2020; Accepted: 13 April 2020; Published: 15 April 2020

check for updates

**Abstract:** The emergence of resistant pathogens is a burden on mankind and threatens the existence of our species. Natural and plant-derived antimicrobial agents need to be developed in the race against antibiotic resistance. Nanotechnology is a promising approach with a variety of products. Biosynthesized silver nanoparticles (AgNP) have good antimicrobial activity. We prepared AgNPs with *trans*-cinnamic acid (TCA) and povidone–iodine (PI) with increased antimicrobial

# References

*pathogens*

MDPI

*Article*

## "Smart" Triiodide Compounds: Does Halogen Bonding Influence Antimicrobial Activities?

Zehra Edis [1,*], Samir Haj Bloukh [1], Hamed Abu Sara [1], Hanusha Bhakhoa [2], Lydia Rhyman [2,3] and Ponnadurai Ramasami [2,3,*]

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Received: 3 September 2019; Accepted: 8 October 2019; Published: 10 October 2019

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**Abstract:** Antimicrobial agents containing symmetrical triiodides complexes with halogen bonding may release free iodine molecules in a controlled manner. This happens due to interactions with the plasma membrane of microorganisms which lead to changes in the structure of the triiodide anion. To verify this hypothesis, the triiodide complex $[Na(12\text{-crown-}4)_2]I_3$ was prepared by an optimized one-pot synthesis and tested against 18 clinical isolates, 10 reference strains of pathogens and five antibiotics. The antimicrobial activities of this symmetrical triiodide complex were determined by zone of inhibition plate studies through disc- and agar-well-diffusion methods. The triiodide complex proved to be a broad spectrum microbicidal agent. The biological activities were related to the calculated partition coefficient (octanol/water). The microstructural analysis of SEM and

# References

processes

MDPI

Article

## Green Synthesis of Potent Antimicrobial Silver Nanoparticles Using Different Plant Extracts and Their Mixtures

May Reda [1], Akram Ashames [1,*], Zehra Edis [1], Samir Bloukh [2], Richie Bhandare [1] and Hamed Abu Sara [2]

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Received: 21 June 2019; Accepted: 2 August 2019; Published: 4 August 2019

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**Abstract:** Nano-sized metals have been introduced as a promising solution for microbial resistance to antimicrobial agents. Silver nanoparticles (AgNPs) have been proven to possess good antimicrobial activity. Green synthesis of AgNPs has been reported as safe, low cost and ecofriendly. This methodology uses extracts originating from different plants to reduce silver ions from $AgNO_3$ into nano-sized particles. In this study, extracts of several plants including ginger, garlic, capsicum and their mixtures were successfully used to produce AgNPs. Numerous spectroscopic, light scattering